



LOMAU.

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Zhu, et al.
Appl. No. : 10/041,688
Filed : January 7, 2002
For : ADHESIVE INCLUDING
MEDICAMENT
Examiner : Ghali, I. A. D.
Group Art Unit : 1615

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DECLARATION OF YONG-HUA ZHU

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, Yong-Hua Zhu, declare as follows:

1. I am a citizen of the United States, residing at 1154 W. Highland Avenue, Redlands, California 92373, and believe that I am the original, first and joint inventor with Wolff M. Kirsch, Cindy Dickson, Min Di Gu, Ghang Zheng Yang, and Qun-Dong Shen of the subject matter which is claimed and for which a patent is sought on the invention entitled "ADHESIVE INCLUDING MEDICAMENT"; the specification of which was filed on January 7, 2002 as Application Serial No. 10/041,688.

2. I have read the Office Action dated October 8, 2004, and understand that the pending claims have been rejected under 35 U.S.C. §103(a) as obvious over WO96/10374 ("WO '374") in view of U.S. 4,919,939 ("US '939") (Claims 1, 4, 5, 8, 12, 13, 16, 17, 20, 26-29, and 31-34), WO '374 in view of US '939 and further in view of US 5,811,091 ("US '091") (Claims 2, 3, 14, and 15), WO '374 in view of US '939 and further in view of WO96/00760 ("WO '760") (Claims 2, 3, 10, 11, 14, 15, and 22-24), or WO '374 in view of US '939 and further in view of WO99/20685 ("WO '685") (Claims 6 and 18).

2. The majority of antibiotics contain active groups which react with cyanoacrylate adhesives. Accordingly, when an antibiotic is directly added to a cyanoacrylate, the antibiotic reacts with the cyanoacrylate such that polymerization occurs and the adhesive immediately

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solidifies, completely losing its adhesive function. Moreover, the antibiotic that reacts with cyanoacrylate becomes deactivated or exhibits a significant degradation in antibiotic activity. The reaction between the antibiotic and cyanoacrylate occurs in the presence or absence of a pore forming agent. Accordingly, the presence of a pore forming agent in the cured adhesive merely facilitates delivery of the deactivated antibiotic to the wound. None of the cited references recognize that interaction between an antibiotic and a cyanoacrylate adhesive can cause immediate polymerization of the adhesive and deactivation of the antibiotic, and none of the references teach a method for preparing stable liquid cyanoacrylate adhesives containing an antibiotic that maintains its effectiveness after being mixed with the cyanoacrylate.

3. I and my co-inventors have discovered that microencapsulation is an effective technique to avoid any undesired chemical interaction between an antibiotic and a cyanoacrylate adhesive, and the resulting deactivation of the antibiotic. When an antibiotic is entrapped in, e.g. a hydrophilic gelatin microcapsule, and then mixed with a cyanoacrylate adhesive, e.g. Super Glue, the microcapsule shell blocks the undesired polymerization reactions because there is no direct contact of the antibiotic and the cyanoacrylate. Our invention enables one to mix a variety of antibiotics with a cyanoacrylate adhesive without interfering interactions between the antibiotic and the cyanoacrylate, yielding a stable liquid adhesive for sealing wounds without loss of antibiotic activity due to reaction between the antibiotic and the cyanoacrylate.

4. I and my co-inventors conducted experiments wherein Penicillin in unencapsulated form was directly mixed with methyl cyanoacrylate adhesive. The methyl cyanoacrylate was observed to solidify within 15 minutes of addition of the unencapsulated antibiotic, thereby destroying the adhesive function of the methyl cyanoacrylate.

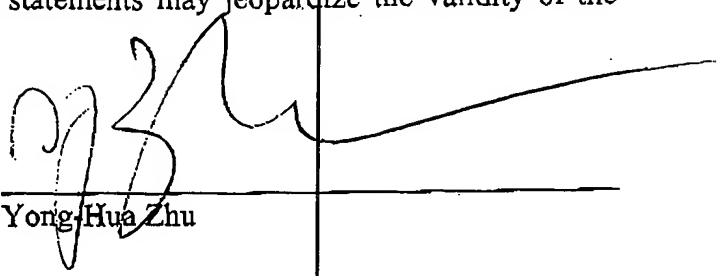
5. I and my co-inventors conducted experiments wherein microencapsulated Penicillin was mixed with the methyl cyanoacrylate adhesive. After mixing, there was no detectable interaction between antibiotic and the methyl cyanoacrylate for at least 10 days, during which time the adhesive maintained its stability, liquidity, good adhesive qualities, and antibiotic activity.

6. I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true. I declare that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the

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United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: 4/6/05


Yong-Hua Zhu

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